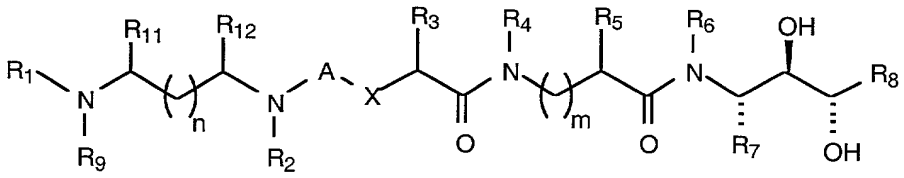
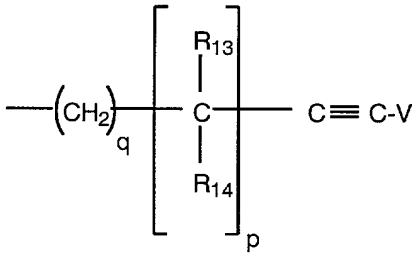
WHAT IS CLAIMED IS:

37. A therapeutic method for preventing hypertension, said method comprising administering to a subject susceptible to such disorder a therapeutically-effective amount of an active compound of Formula I:



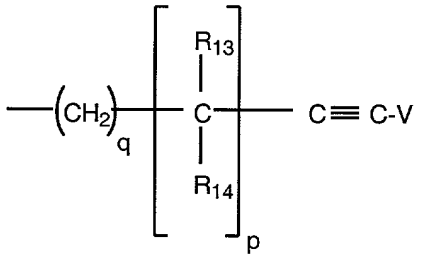
(I)

wherein A is selected from methylene, CO, SO and SO_2; wherein X is selected from oxygen atom, methylene and $>NR_{10}$ with R_{10} selected from hydrido, alkyl and benzyl; wherein each of R_1 and R_9 is a group independently selected from hydrido, alkyl, cycloalkyl, alkoxyacyl, haloalkyl, alkoxycarbonyl, benzyloxycarbonyl, loweralkanoyl, haloalkylacyl, phenyl, benzyl, naphthyl, and naphthylmethyl, any one of which groups having a substitutable position may be optionally substituted with one or more radicals selected from alkyl, alkoxy, alkenyl, alkynyl, halo, haloalkyl, cyano and phenyl, and wherein the nitrogen atom to which R_1 and R_9 are attached may be combined with oxygen to form an N-oxide; wherein R_2 is selected from hydrido, alkyl, dialkylaminoalkyl, alkylacylaminoalkyl, benzyl and cycloalkyl; wherein R_3 is selected from alkyl, cycloalkylalkyl, acylaminoalkyl, phenylalkyl, naphthylmethyl, aryl, heterocyclicalkyl and heterocycliccycloalkyl, wherein the cyclic portion of any of said phenylalkyl, naphthylmethyl, aryl, heterocyclicalkyl and heterocycliccycloalkyl groups may be substituted by one or more radicals selected from halo, hydroxy, alkoxy and alkyl; wherein each of R_4 and R_6 is independently selected from hydrido, alkyl, benzyl and cycloalkyl; wherein each of R_5 and R_8 is independently selected from



wherein V is selected from hydrido, alkyl, cycloalkyl, haloalkyl, benzyl and phenyl; wherein each of R_{13} and R_{14} is a radical independently selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, phenyl, heterocyclic, heterocyclicalkyl and heterocycliccycloalkyl; wherein R_7 is selected from substituted or unsubstituted alkyl, cycloalkyl, phenyl, cycloalkylalkyl and phenylalkyl, any one of which may be substituted with one or more groups selected from alkyl, hydroxy, alkoxy, halo, haloalkyl, alkenyl, alkynyl and cyano; wherein each of R_{11} and R_{12} is independently selected from hydrido, alkyl, haloalkyl, dialkylamino and phenyl; and wherein m is zero or one; wherein n is a number selected from zero through five; wherein p is a number selected from zero through five; and wherein q is a number selected from zero through five; or a pharmaceutically-acceptable salt thereof.

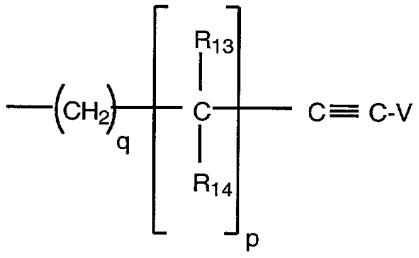
38. The method of Claim 37 wherein A is selected from methylene, CO, SO and SO_2; wherein X is selected from oxygen atom, methylene and $>NR_{10}$ with R_{10} selected from hydrido, alkyl and benzyl; wherein each of R_1 and R_9 is independently selected from hydrido, lower alkyl, haloalkyl, cycloalkyl, alkoxycarbonyl, benzyloxycarbonyl, loweralkanoyl, alkoxyacyl, phenyl and benzyl, and wherein the nitrogen atom to which R_1 and R_9 are attached may be combined with oxygen to form an N-oxide; wherein each of R_2, R_4 and R_6 is independently selected from hydrido and alkyl; wherein R_3 is selected from phenylalkyl, naphthylmethyl, cyclohexylalkyl, cyclopentylalkyl, heteroarylalkyl and heteroarylcycloalkyl; wherein each of R_5 and R_8 is independently selected from



wherein V is selected from hydrido, alkyl, haloalkyl, benzyl and phenyl; wherein each of R_{13} and R_{14} is a radical independently selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, heteroarylalkyl and heteroarylcycloalkyl; wherein R_7 is selected from substituted or unsubstituted cyclohexylmethyl and benzyl, either one of which may be substituted with one or more groups selected from alkyl, hydroxy, alkoxy, halo and haloalkyl; wherein each of R_{11} and R_{12} is independently selected from hydrido, alkyl, dialkylamino and phenyl; wherein m is zero or one; wherein n is a number selected from zero through five; wherein p is a number selected from zero through five; and wherein q is a number selected from zero through five; or a pharmaceutically-acceptable salt thereof.

39. The method of Claim 38 wherein A is selected from methylene, CO, SO and SO_2; wherein X is selected from oxygen atom, methylene and $>NR_{10}$ with R_{10} selected from hyrido, alkyl and benzyl; wherein each of R_1 and R_9 is independently selected from hydrido, alkyl, alkoxyacyl, haloalkyl, alkoxycarbonyl, benzyloxycarbonyl and benzyl, and wherein the nitrogen atom to which R_1 and R_9 are attached may be combined with oxygen to form an N-oxide; wherein each of R_2, R_4 and R_6 is independently selected from hydrido and alkyl; wherein R_3 is selected from benzyl, phenethyl, cyclohexylmethyl, phenpropyl, pyrrolidinyl, piperidinyl, pyrrolidinylmethyl, piperidinylmethyl, pyrazolemethyl, pyrazoleethyl, pyridylmethyl, pyridylethyl, thiazolemethyl, thiazoleethyl, imidazolemethyl, imidazoleethyl, thienylmethyl, thienylethyl, furanylmethyl, furanylethyl,

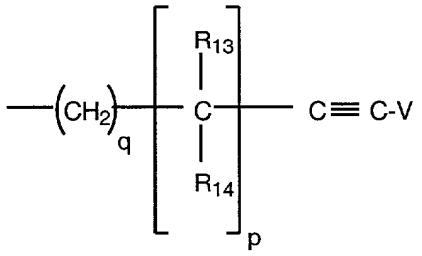
oxazolemethyl, oxazoleethyl, isoxazolemethyl, isoxazoleethyl, pyridazinemethyl, pyridazineethyl, pyrazinemethyl and pyrazineethyl; wherein each of R_5 and R_8 is independently selected from



wherein V is selected from hydrido, alkyl and haloalkyl; wherein each of R_{13} and R_{14} is a radical independently selected from hydrido, alkyl, alkenyl, alkynyl, thiazole and thiazolemethyl; wherein R_7 is cyclohexylmethyl; wherein each of R_{11} and R_{12} is independently selected from hydrido, alkyl, dialkylamino and phenyl; wherein m is zero or one; wherein n is a number selected from zero through five; wherein p is a number selected from zero through five; and wherein q is a number selected from zero through five; or a pharmaceutically-acceptable salt thereof.

40. The method of Claim 39 wherein A is selected from CO and SO_2; wherein X is selected from oxygen atom, methylene and $>NR_{10}$ with R_{10} selected from hydrido and methyl; wherein each of R_1 and R_9 is independently selected from hydrido, lower alkyl, alkoxyacyl, alkoxycarbonyl, benzyloxycarbonyl, haloalkyl and benzyl, and wherein the nitrogen atom to which R_1 and R_9 are attached may be combined with oxygen to form an N-oxide; wherein R_2 is selected from hydrido, methyl, ethyl and isopropyl; wherein R_3 is selected from benzyl, phenethyl, cyclohexylmethyl, pyrrolidinyl, piperidinyl, pyrrolidinylmethyl, piperidinylmethyl, pyrazolemethyl, pyrazoleethyl, pyridylmethyl, pyridylethyl, thiazolemethyl, thiazoleethyl, imidazolemethyl, imidazoleethyl, thienylmethyl, thienylethyl, furanylmethyl, furanylethyl, oxazolemethyl, oxazoleethyl, isoxazolemethyl, isoxazoleethyl,

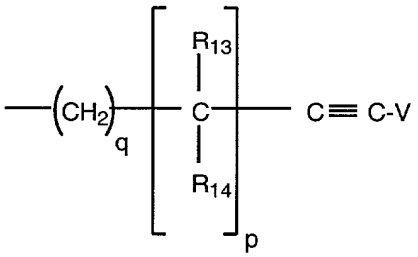
pyridazinemethyl, pyridazineethyl, pyrazinemethyl and pyrazineethyl; wherein each of R_4 and R_6 is independently selected from hydrido and methyl; wherein each of R_5 and R_8 is independently selected from



wherein V is selected from hydrido, alkyl and trifluoromethyl; wherein each of R_{13} and R_{14} is a radical independently selected from hydrido, alkyl and alkynyl; wherein R_7 is cyclohexylmethyl; wherein each of R_{11} and R_{12} is independently selected from hydrido, alkyl, dialkylamino and phenyl; wherein m is zero; wherein n is a number selected from zero through five; wherein p is a number selected from zero through five; and wherein q is a number selected from zero through five; or a pharmaceutically-acceptable salt thereof.

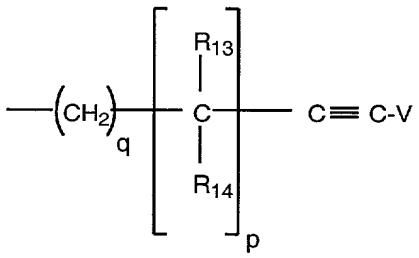
41. The method of Claim 40 wherein A is selected from CO and SO_2; wherein X is selected from oxygen atom and methylene; wherein each of R_1 and R_9 is independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, benzyl, b, b, b-trifluoroethyl, t-butyloxycarbonyl and methoxymethylcarbonyl, and wherein the nitrogen atom to which R_1 and R_9 are attached may be combined with oxygen to form an N-oxide; wherein R_2 is selected from hydrido, methyl, ethyl and isopropyl; wherein R_3 is selected from benzyl, cyclohexylmethyl, phenethyl, pyrazolemethyl, pyrazoleethyl, pyridylmethyl, pyridylethyl, thiazolemethyl, thiazoleethyl, imidazolemethyl, imidazoleethyl, thienylmethyl, thienylethyl, furanylmethyl, furanylethyl, oxazolemethyl, oxazoleethyl, isoxazolemethyl, isoxazoleethyl, pyridazinemethyl,

pyridazineethyl, pyrazinemethyl and pyrazineethyl; wherein each of R_5 and R_8 is independently selected from



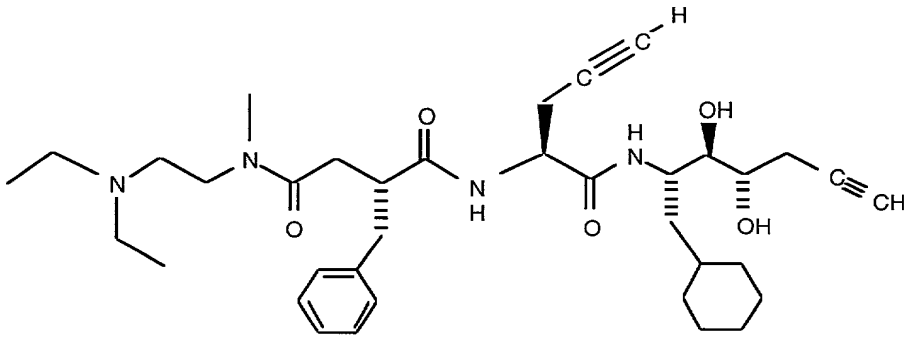
wherein V is selected from hydrido, alkyl and trifluoromethyl; wherein each of R_{13} and R_{14} is a radical independently selected from hydrido, methyl, ethyl, propyl and ethynyl; wherein R_7 is cyclohexylmethyl; wherein each of R_4 and R_6 is independently selected from hydrido and methyl; wherein each of R_{11} and R_{12} is independently selected from hydrido, alkyl, dialkylamino and phenyl; wherein m is zero; wherein n is a number selected from zero through five; wherein p is a number selected from zero through five; and wherein q is a number selected from zero through five; or a pharmaceutically-acceptable salt thereof.

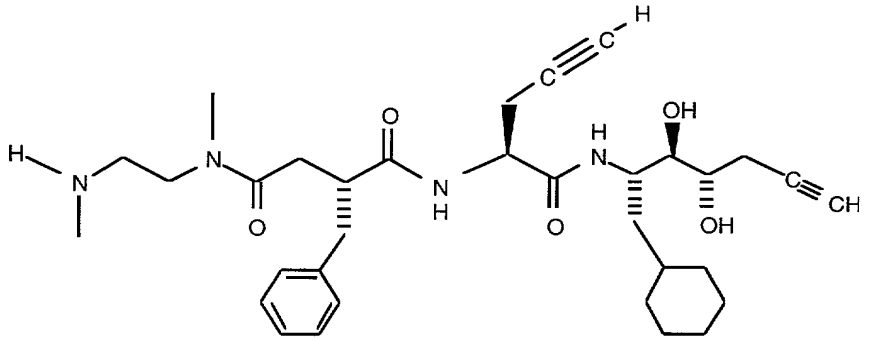
42. The method of Claim 41 wherein A is selected from CO and SO_2; wherein X is selected from oxygen atom and methylene; wherein each of R_1 and R_9 is a group independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, benzyl, b, b, b-trifluoroethyl, t-butyloxycarbonyl and methoxymethylcarbonyl, and wherein the nitrogen atom to which R_1 and R_9 are attached may be combined with oxygen to form an N-oxide; wherein R_2 is selected from hydrido, methyl, ethyl and isopropyl; wherein R_3 is selected from benzyl, cyclohexylmethyl, phenethyl, imidazolemethyl, pyridylmethyl and 2-pyridylethyl; wherein each of R_5 and R_8 is independently selected from

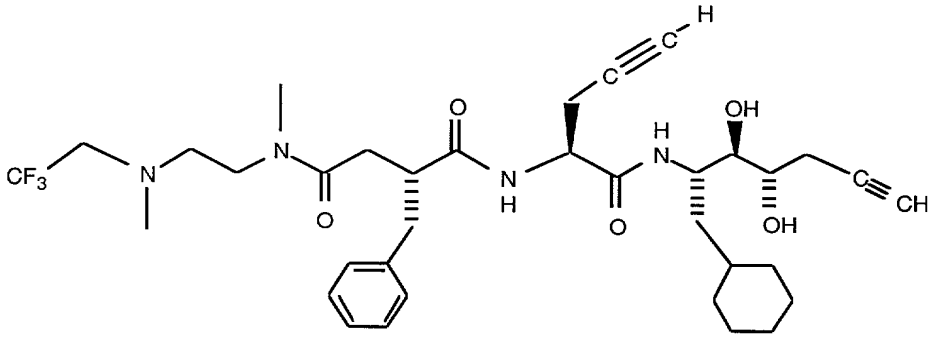


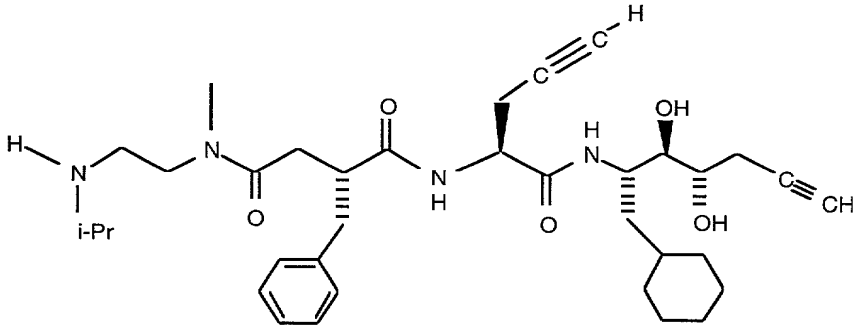
wherein V is selected from hydrido, alkyl and trifluoromethyl; wherein each of R_{13} and R_{14} is a radical independently selected from hydrido, methyl and ethynyl; wherein R_7 is cyclohexylmethyl; wherein each of R_4 and R_6 is independently selected from hydrido and methyl; wherein each of R_{11} and R_{12} is independently selected from hydrido, alkyl and phenyl; wherein m is zero; wherein n is a number selected from zero through three; wherein p is a number selected from one through three; and wherein q is zero or one; or a pharmaceutically-acceptable salt thereof.

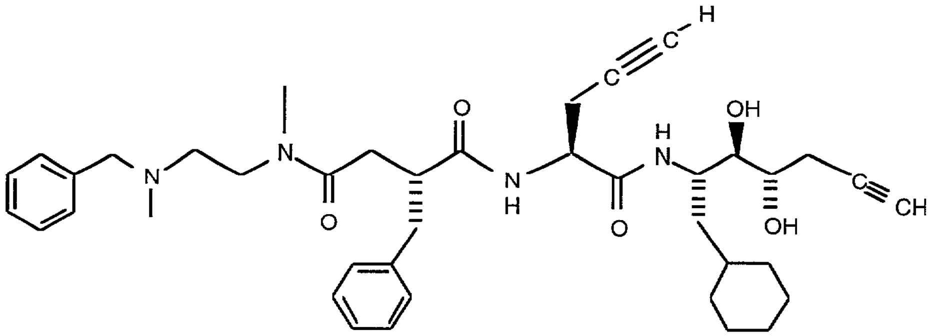
43. The method of Claim 42 wherein said compound is selected from compounds, their tautomers, and the pharmaceutically-acceptable esters and salts thereof, of the group consisting of

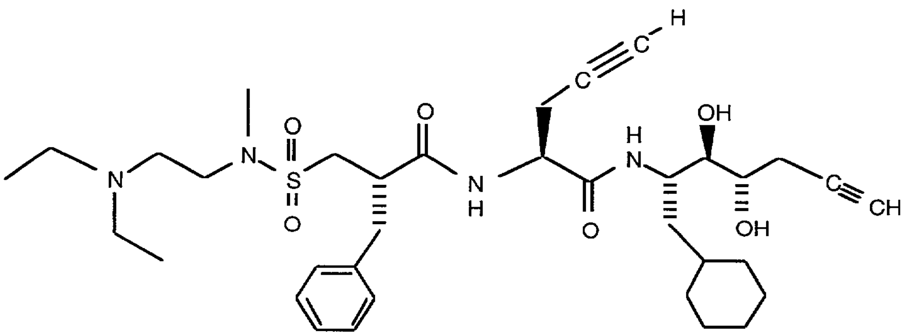


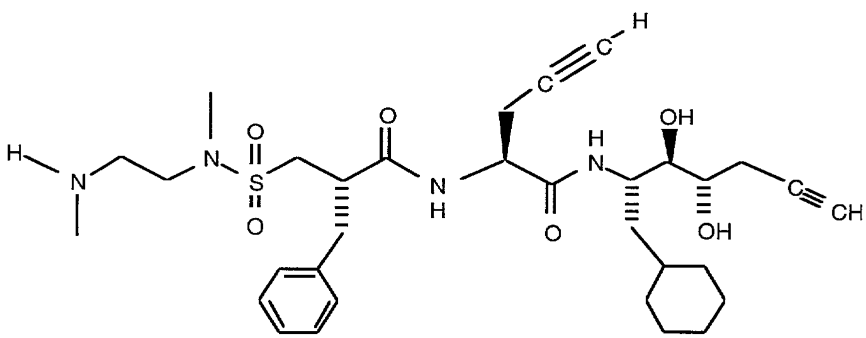


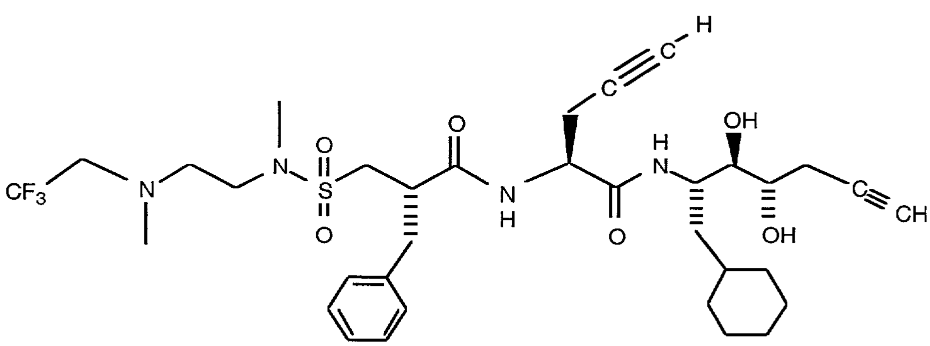


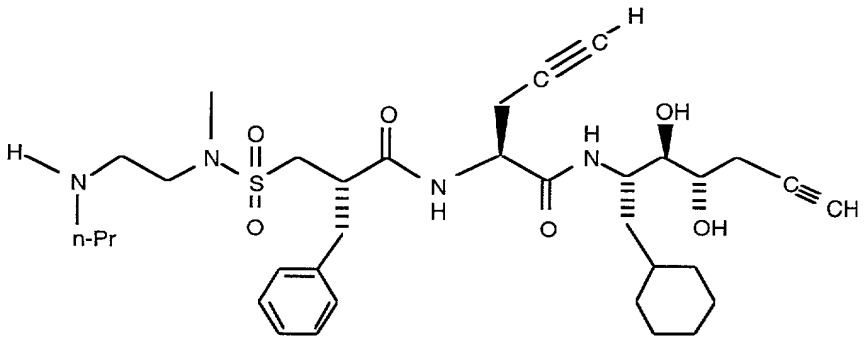


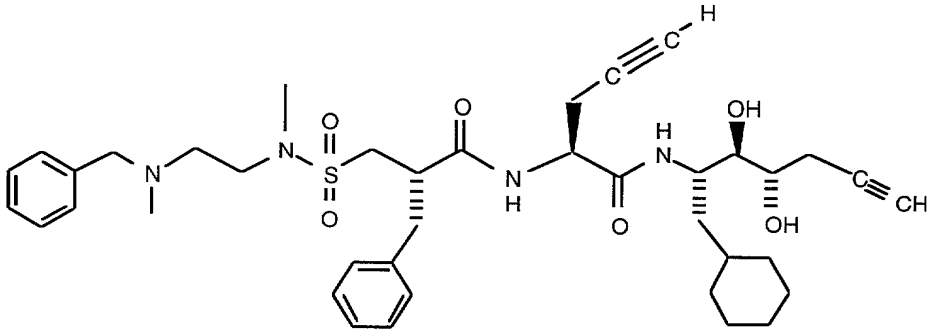


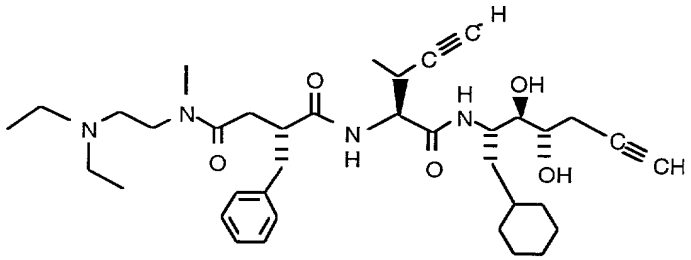


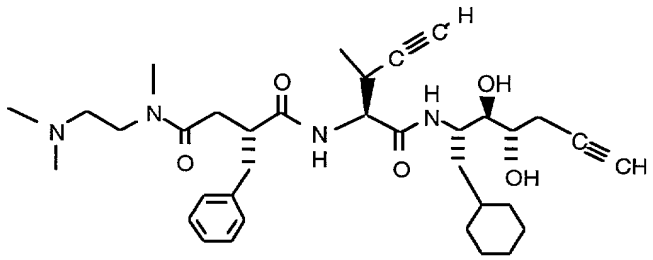


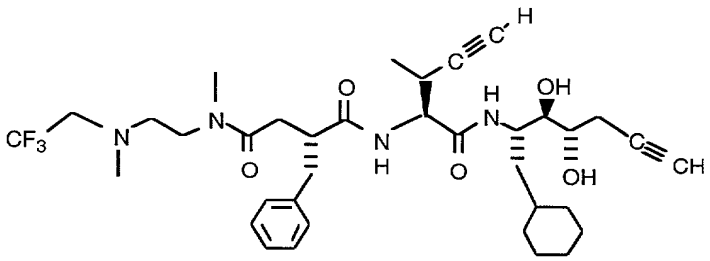


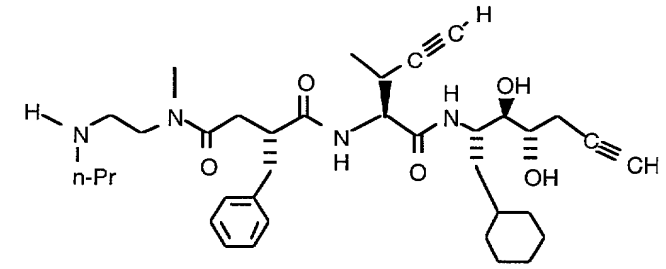


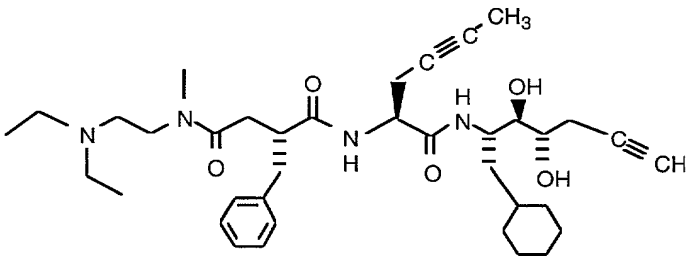


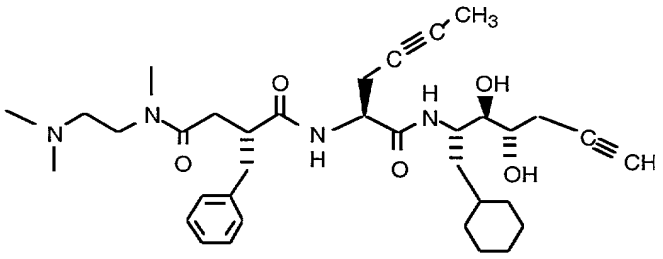


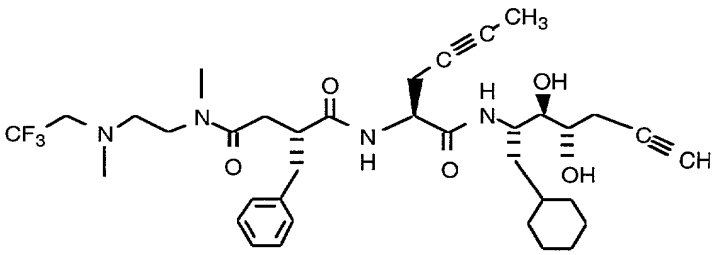


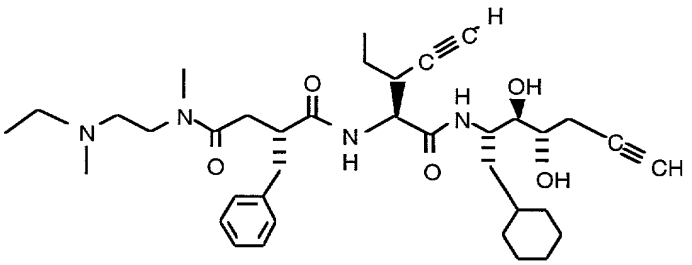


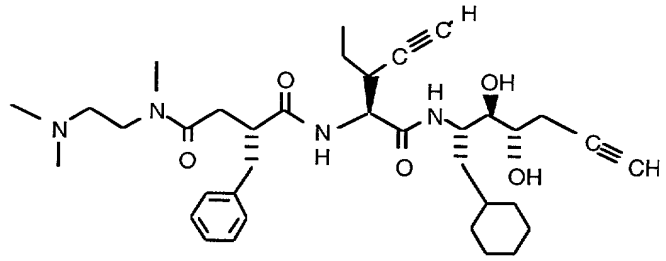


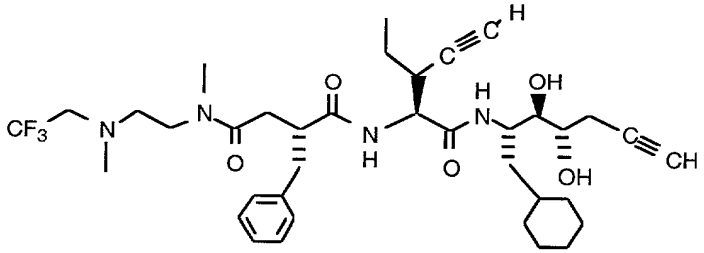


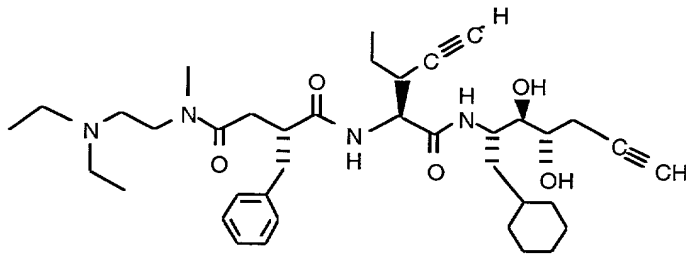


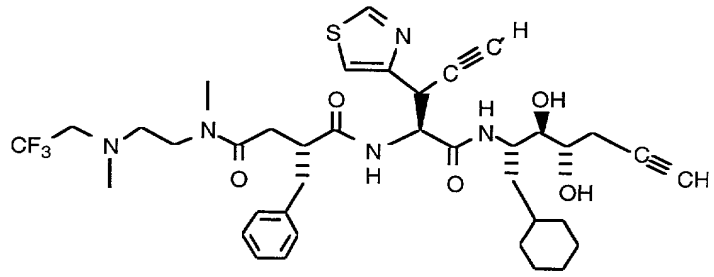


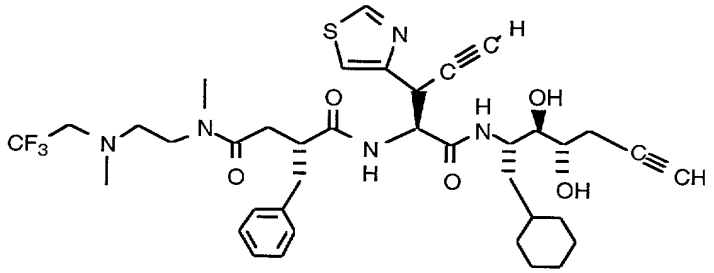


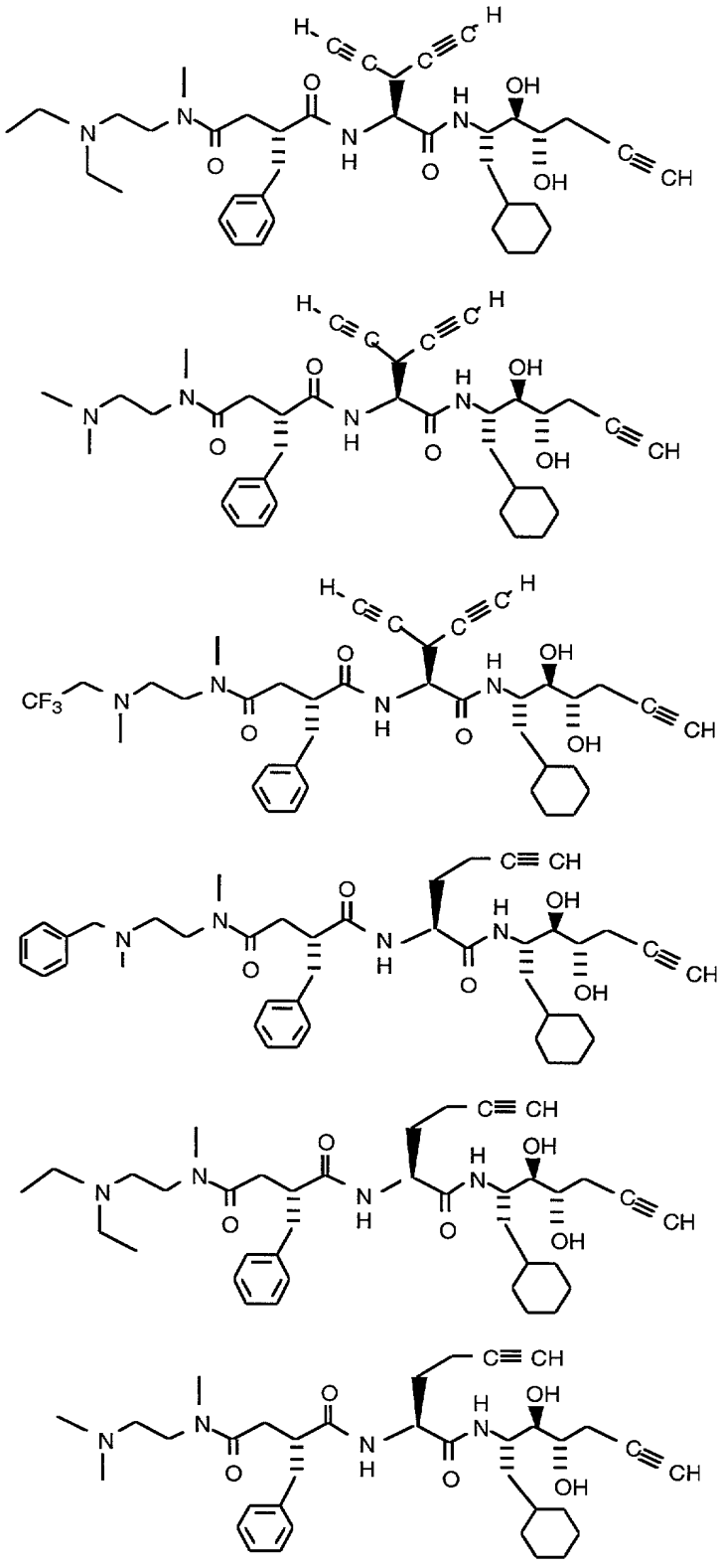


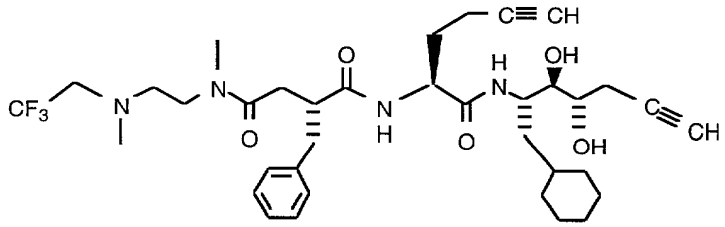




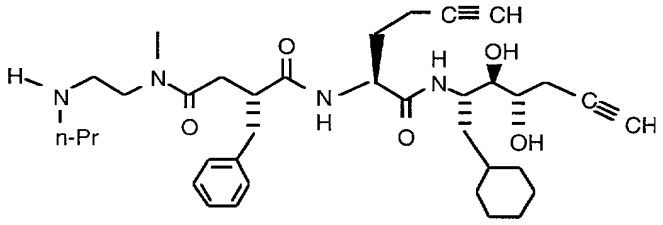








and

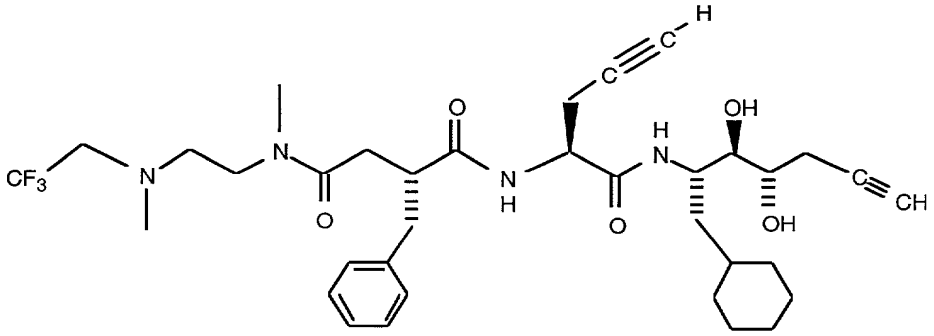


.

44. The method of Claim 42 wherein said compound is N1-[1R*-[[[1S,1R*-(cyclohexylmethyl)-2S*,3R*-dihydroxy-hexynyl]amino]carbonyl]-3-butynyl]-N4-[2-(dimethylamino)ethyl]-N4-methyl-2S*-(phenylmethyl)butanediamide or a pharmaceutically-acceptable salt thereof.

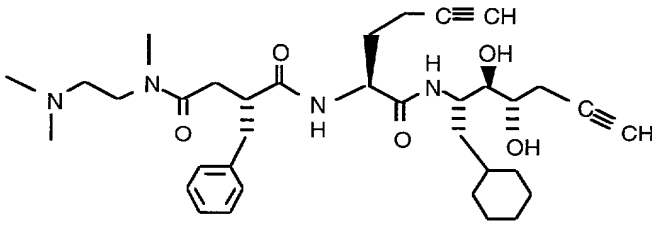
45. The method of Claim 42 wherein said compound is [1R*-[[[1R*-[[[1S,1R*-(cyclohexylmethyl)-2S*,3R*-dihydroxy-hexynyl]amino]carbonyl]-3-butynyl]amino]carbonyl]-2-phenylethyl)[2-(dimethylamino)ethyl]methylcarbamate or a pharmaceutically-acceptable salt thereof.

46. The method of Claim 42 wherein said compound is



or a pharmaceutically-acceptable salt thereof.

47. The method of Claim 42 wherein said compound is

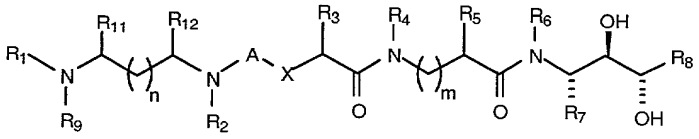


or a pharmaceutically-acceptable salt thereof.

USE OF PROPARGYL GLYCINE AMINO PROPARGYL DIOL COMPOUNDS FOR PREVENTION OF HYPERTENSION

ABSTRACT

Compounds characterized generally as propargyl glycine amino propargyl diol derivatives are useful for prevention of hypertension. Compounds of particular interest are those of Formula I



(I)

wherein A is selected from CO and SO_2 wherein X is selected from oxygen atom and methylene; wherein each of R_1 and R_9 is a group independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, benzyl, b, b, b-trifluoroethyl, t-butyloxycarbonyl and methoxymethylcarbonyl, and wherein the nitrogen atom to which R_1 and R_9 are attached may be combined with oxygen to form an N-oxide; wherein R_2 is selected from hydrido, methyl, ethyl and isopropyl; wherein R_3 is selected from benzyl, cyclohexylmethyl, phenethyl, imidazolemethyl, pyridylmethyl and 2-pyridylethyl; wherein each of R_5 and R_8 is independently propargyl or a propargyl-containing moiety; wherein R_7 is cyclohexylmethyl; wherein each of R_4 and R_6 is independently selected from hydrido and methyl; wherein each of R_{11} and R_{12} is independently selected from hydrido, alkyl and phenyl; wherein m is zero; and wherein n is a number selected from zero through three; or a pharmaceutically-acceptable salt thereof.

United States Patent & Trademark Office

Office of Initial Patent Examination -- Scanning Division

Application deficiencies found during scanning:

☐ Page(s)__________ of ______________________________ were not present for scanning.
(Document title)

☐ Page(s)__________ of ______________________________ were not present for scanning.
(Document title)

page 35 To 65 As Part of Spec are Table

▫ ***Scanned copy is best available.***